

### ***Remarks***

#### ***Support for the Amendments***

Support for the amendments to claims 52, 53, 72 and 73 can be found throughout the present specification, specifically at page 51, paragraph 96; at page 66, paragraph 158 through page 68, paragraph 160; at page 80, paragraph 190 through page 81, paragraph 191; and throughout the Examples and Drawings. Support for new claims 88-97 can be found throughout the specification, specifically at page 51, paragraph 96; at page 66, paragraph 158 through page 68, paragraph 160; at page 80, paragraph 190 through page 81, paragraph 191; and throughout the Examples and Drawings. Hence, these amendments do not introduce new matter, and their entry and consideration are respectfully requested.

#### ***Status of the Claims***

By the foregoing amendments, claims 52, 53, 72 and 73 have been amended and new claims 88-97 are sought to be entered. Upon entry of the foregoing amendments, claims 46-97 are pending in the application, with claims 46, 65 and 86 being the independent claims.

#### ***Summary of the Office Action***

In the Office Action dated June 29, 2004, the Examiner has made one objection to, and three rejections of, the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***The Rejection Under 35 U.S.C. § 102(b) over Shuman***

In the Office Action at page 2, the Examiner has rejected claims 65, 67-71, 74-82 and 84 under 35 U.S.C. § 102(b), as allegedly being anticipated by Shuman (*J. Biol. Chem.* 269:32678-32684 (1994); hereinafter "Shuman"). Applicants respectfully traverse this rejection.

The Examiner contends that essentially any DNA sequence might undergo general (homologous) recombination, and that Shuman discloses a nucleic acid molecule comprising a topoisomerase site that is 0 to 100 nucleotides from such a DNA sequence, and therefore concludes that Shuman discloses the presently claimed invention. Applicants respectfully disagree with this conclusion.

Applicants respectfully submit that the ordinarily skilled artisan would readily understand that the term "recombination site" as it is used in the present claims and specification refers to site-specific recombination sites. The Examiner's attention is directed to the present specification at page 67, paragraph 160, where the term "recombination site" is defined. "Recombination sites are discrete sections or segments of nucleic acid on the participating nucleic acid molecules that are recognized and bound by a site-specific recombination protein during the initial stages of integration or recombination." Specification at page 67, paragraph 160, lines 3-6. Applicants respectfully submit that the ordinarily skilled artisan would readily understand that the term "recombination site," as it is used in the present claims and specification, refers to site-specific recombination sites, rather than *any* DNA sequence that might undergo general (homologous) recombination as the Examiner contends. Several non-limiting examples of site-specific recombination sites are

given throughout the present specification (*see e.g.*, Specification at page 80, paragraph 190)).

Applicants respectfully submit that Shuman does not disclose an isolated nucleic acid molecule comprising a recombination site, much less an isolated nucleic acid molecule comprising a first recombination site and a second recombination and a topoisomerase recognition site, as recited in present claim 65 (and hence claims 67-71, 74-82 and 84 that depend ultimately therefrom).

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984); *see also PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566 (Fed. Cir. 1996) ("[t]o anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter."). The disclosure of Shuman does not meet this burden.

Applicants respectfully submit therefore that Shuman does not disclose the subject matter of the present claims. In view of the foregoing remarks, and in view of *Kalman*, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 65, 67-71, 74-82 and 84 under 35 U.S.C. § 102(b) over Shuman.

***The Rejection Under 35 U.S.C. § 112, First Paragraph***

In the Office Action at page 3, the Examiner has rejected claims 52 and 72 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Applicants respectfully traverse this rejection

For reasons unrelated to this rejection, by the foregoing amendments, claims 52 and 72 have been amended to remove the reference to mutants, variants and derivatives. Thus, this rejection has been rendered moot. Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, of claims 52 and 72, be reconsidered and withdrawn.

***The Rejections Under 35 U.S.C. § 112, Second Paragraph***

In the Office Action at pages 3-4, the Examiner has rejected claims 52, 53, 72 and 73 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

For reasons unrelated to this rejection, by the foregoing amendments, claims 52, 53, 72 and 73 have been amended to remove the reference to mutants, variants and derivatives. Thus, this rejection has been rendered moot. Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn

***The Objection to Claims 66 and 85***

In the Office Action at page 2, the Examiner has objected to claims 66 and 85, indicating that these claims depend from a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants acknowledge this designation of provisionally allowable subject matter. Applicants respectfully submit that, in view of the foregoing amendments and remarks, all of the currently pending claims are in condition for allowance. Reconsideration and withdrawal of this objection are respectfully requested.

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***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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